

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ



Year 2

**Endocrine and genitourinary
module**

I want to get pregnant

Basic Science Principles for Clinical Reasoning

- 1- **Critical thinking**
- 2- Introduction to **common forms of disease**
- 3- How basic sciences help understanding
- 4- **Respect** patient's complaint & symptoms
- 5- Create questions
- 6- **Problem solving**
- 7- **Building teams** interpersonal skills

Dealing with

Case co-ordinator

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*"All of life is
a constant
education."*

ELEANOR ROOSEVELT

I want to get pregnant



Laila is a 37-year-old female. She is married to Roshdy who is 37-years-old. They were married 7 years ago. They presented to the infertility clinic with the complaint of inability to conceive for the **last 2 years**.



Laila has a 5-years-old daughter. Laila reports good health and no problems in conceiving her previous pregnancy or in the vaginal delivery of her daughter.

I want to get pregnant



Roshdy has no medical problems or past surgery. He works as a long-distance **truck driver** and is on the road 1-2 weeks each month. He smokes a pack of cigarettes a day since age 18. He occasionally uses **amphetamines** to stay awake while driving at night.



The couple has sexual intercourse 3-5 times per week when he is at home.

I want to get pregnant



The doctor asked Laila about her **menstrual cycle** and whether she has taken any **contraception**.

Laila said that she used **birth control pills** until 2 years ago. The couple has been trying to conceive since then and report a high degree of stress related to their lack of success.



She reported that her periods were regular on the birth control pills, but has been irregular since she discontinued taking them. She reports having **periods every 5-7 weeks**.

I want to get pregnant



Past history is remarkable only for mild depression. She has been taking

Imipramine for the last year.

Laila has **no** history of **sexual transmitted diseases** and **no abnormal Paps**.

No smoking, no alcohol or other drug intake.

She has had no surgery.

The doctor asked her about any discharge from the breast. Laila said that she occasionally has transparent or whitish **breast discharge**

Examination

Laila is 160cm in height and weighs 90 kilos.

Vital signs: within normal

Breast examination: revealed no tenderness or masses, but **bilateral galactorrhea on compression of the areola**.

Pelvic exam reveals normal genitalia, well-estrogenized vaginal vault mucosa and cervical mucus consistent with the proliferative phase.

The uterus is anteflexed and normal in size without masses or tenderness.

Discussion

Laila and Roshdy who are 37 years old presented to the infertility clinic with the complaint of inability to conceive for the last **2 years**.

1- Is this duration significant?

Explain

Definition of infertility

1. No **conception** +
2. Regular sexual **intercourse** +
3. Unprotected sexual intercourse with No **contraception**
4. For **One** year

Types

1. Primary infertility (never pregnant) =
1/3 of cases

2. Secondary infertility (Previous pregnancy) = **2/3 of cases**

- This duration is significant as this is a case of secondary infertility
- In secondary infertility the significant period of infertility reduced to 6 months not one year

Chances of conception

Half of those who do not conceive in the first year
will do so in the second year
(cumulative pregnancy rate over 90%)

The chances of conceiving in any given menstrual cycle is
less than 20%

2- List the couple's problems

List the couple's problems

Female problems

1. Oligomenorrhea
2. Galactorrhea (hyperprolactinemia)
3. Using antidepressant drugs
4. High BMI

Male problems

1. Occupational problems as a truck driver which affect spermatogenesis
2. Using spermatotoxic drugs as amphetamine
3. Smoking

- **Sexual problems for both of them**
- **Absence of sexual intercourse for 2 weeks or more due to the nature of his occupation**

Laila and Roshdy reported good health with no problems with intercourse nor prior urogenital infections or exposure to sexually transmitted diseases STDs.

3- a. Why did the doctor ask about urogenital infections?

b. What are the common sexually transmitted diseases?

c. What other infections may affect fertility?

Factors affecting Fertility

STDs and Other Infections

- **Gonococci (causing gonorrhea) and Chlamydia trachomatis D-K (causing non-gonococcal urethritis) can lead to:**
 - **in women: cervicitis, salpingitis, and pelvic inflammatory disease (major cause of tubal infertility)**
 - **in men: urethritis, epididymitis, accessory gland infection**
- **Other infections that may affect fertility include:**
- **Mumps, leading to orchitis, may cause secondary testicular atrophy**
- **Tuberculosis, toxoplasmosis, malaria, schistosomiasis and leprosy**

Roshdy works as a long-distance **truck driver** and is on the road 1-2 weeks each month.

4- Is there a relation between occupation and male fertility?

Toxic Agents For spermatogenesis

The effect is dose related, and is reversible with many cases:

Occupational hazards:

- *Working with heavy metals:*

Occupational hazards: battery workers, painters, welding processes.

- *Exposure to high temperatures:* Smelters.

- *Exposure to pesticides.*

- *Exposure to chemical toxic agents:* Textile industry, Plastic manufacture, Dry cleaning

- *Exposure to radioactive materials.*

Unhealthy habits:

Unhealthy habits:

Heavy smoking.

Alcoholism.

Addiction e.g.

cannabis.

Therapeutic agents:

He occasionally uses **amphetamines** to stay awake while driving at night.

5- Is the drug history important in Roshdy?

Drug history is important in this case□

As some drugs affect fertility and this effect is reversible with most of them

1- Chemotherapeutic agents: these induce germinal epithelial aplasia

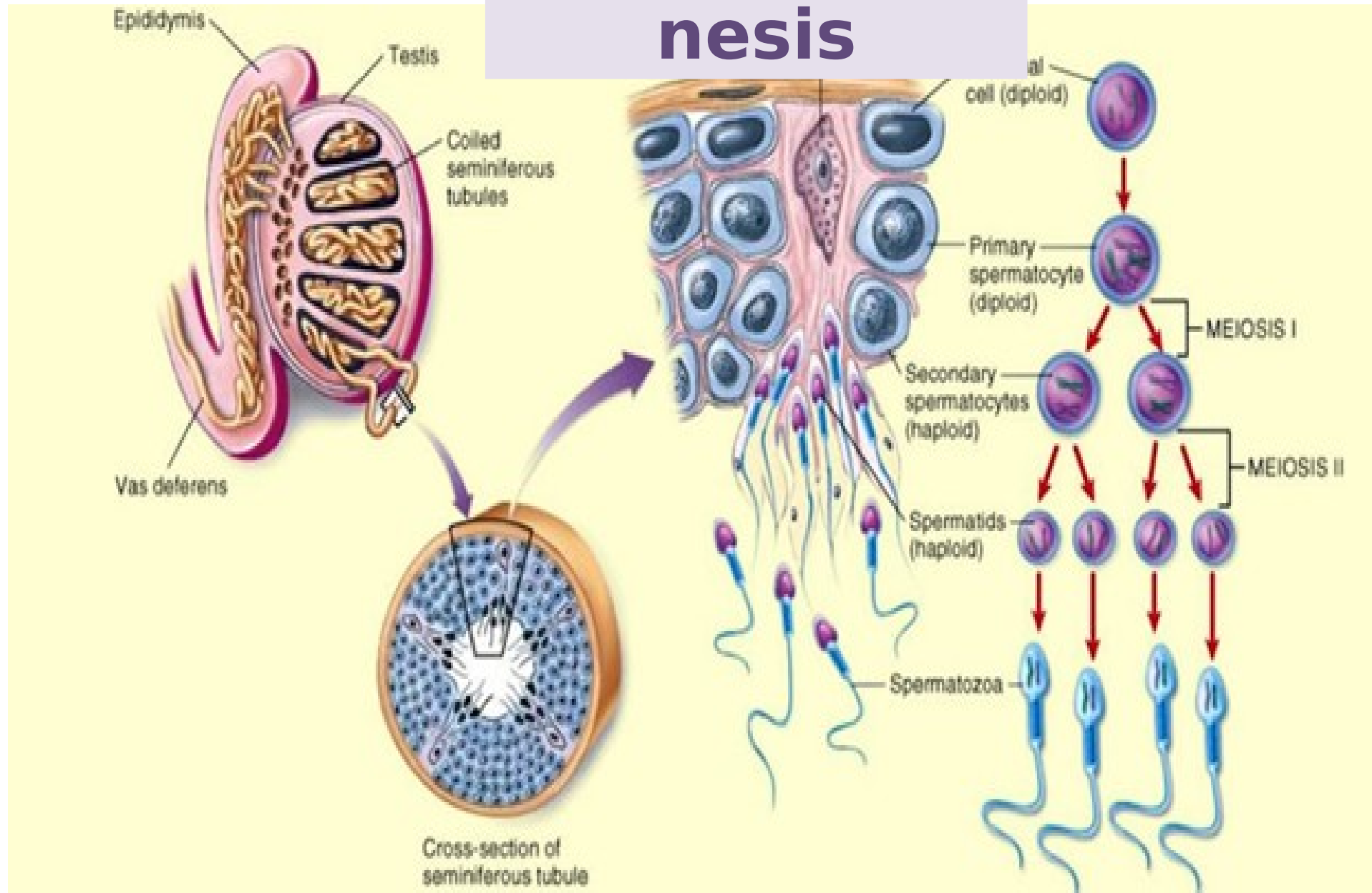
Methotrexate , cisplatin

2- Depression of spermatogenesis is possible with the following drugs:

spironolactone, ketoconazole , cimetidine , anti-malarial drugs, corticosteroids, salicylic acid derivatives, sulfasalazine, anabolic steroids, amphetamines,,

What are the steps of spermatogenesis and factors affecting it?

Spermatogenesis



Roshdy is on the road 1-2 weeks each month.

6- Interpret

Fertile Period in Female Sexual Cycle:

- ✓ The **ovum** remains viable and capable of being fertilized after it is expelled from the ovary probably no longer than 24 hours.
- ✓ The **sperm** remain fertile in the female reproductive tract for up to 5 days.
- ✓ Therefore, for fertilization to occur the sperm must be available soon after ovulation. Thus, sexual intercourse must occur ***between 4 and 5 days before ovulation up to a few hours after ovulation.***

Laila said that she used birth control pills until 2 years ago.

7- What is the nature of contraceptive pills?

1-Combined OCP: estrogen
+progestins

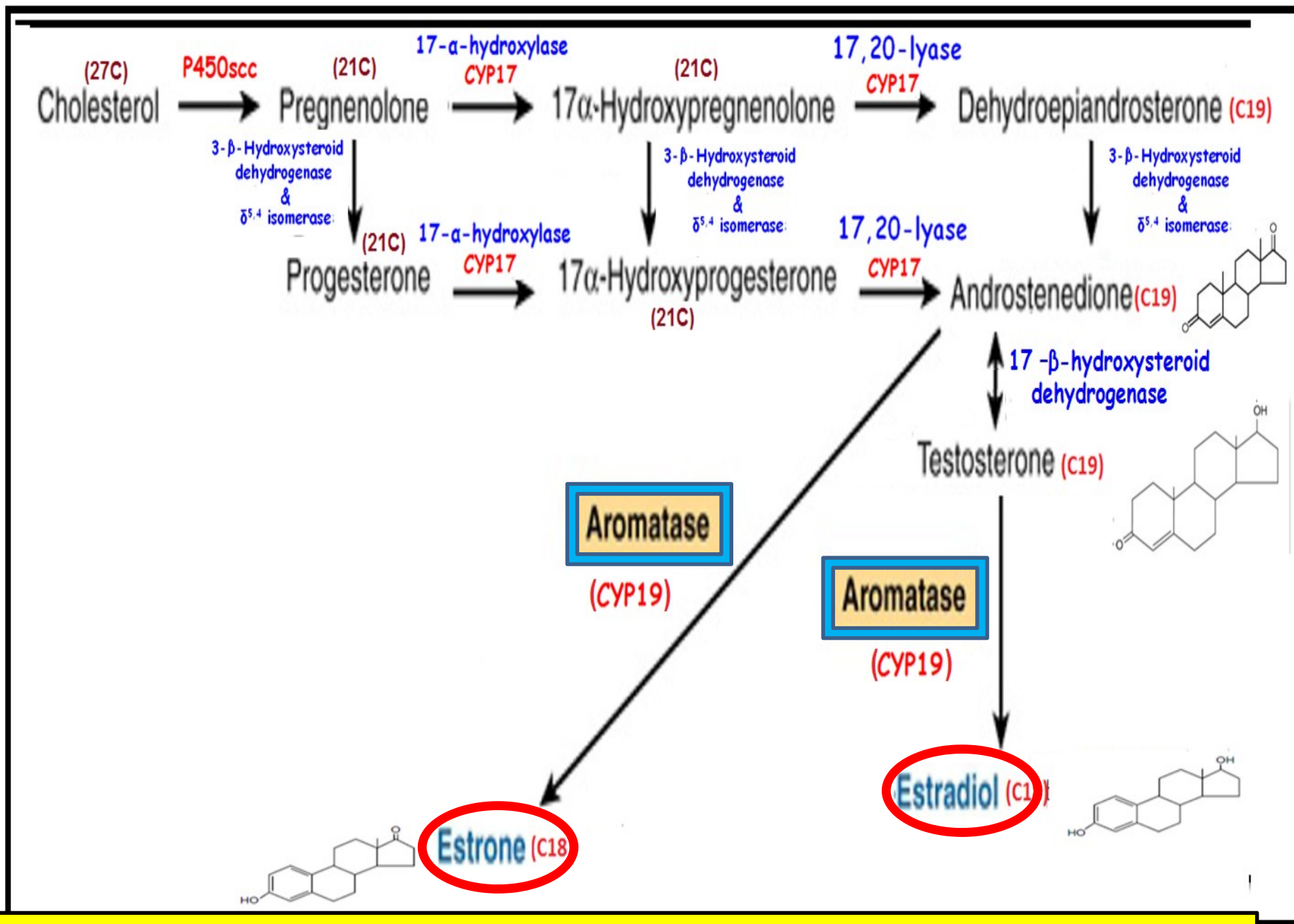
2- Progestin only (mini-pill)



Contraceptive pills are hormonal in nature

What hormones are produced by the ovary?

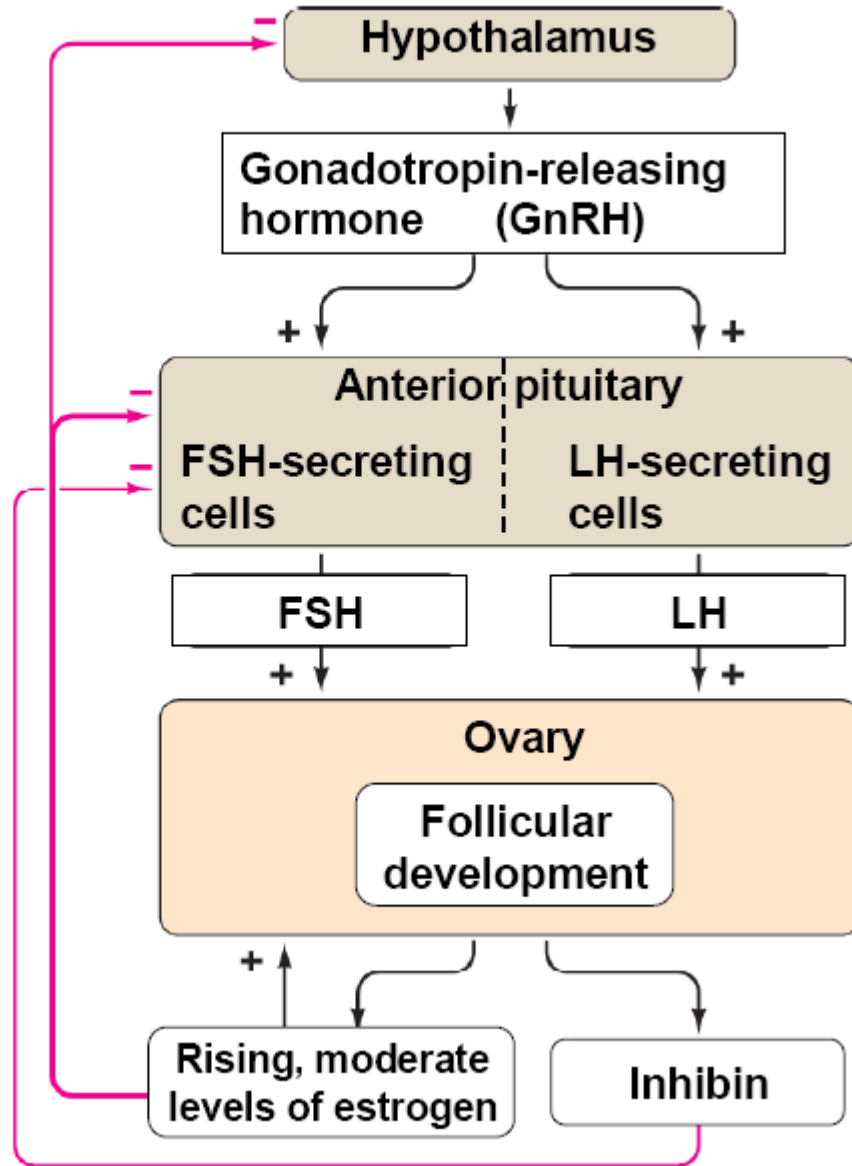
What are the steps of their synthesis ?



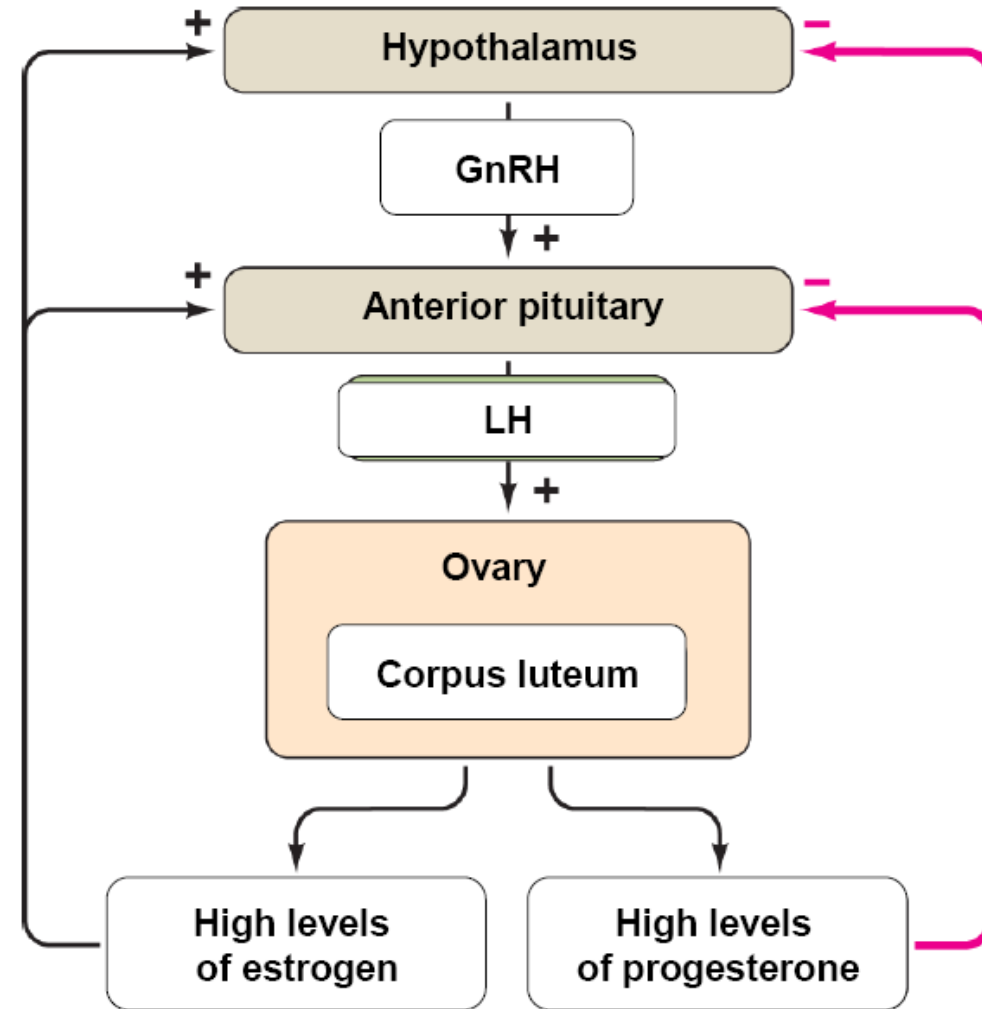
Estradiol, is the predominant and most potent of the ovarian estrogens

8- How could estrogen hormone act as a contraceptive?

Control of Ovarian hormones



During Follicular phase



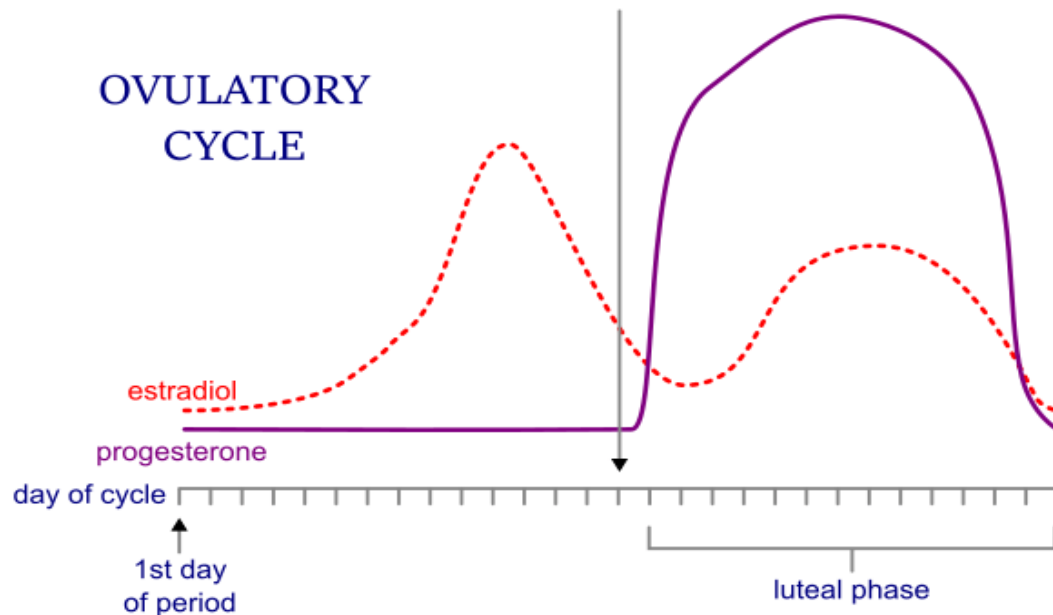
During Luteal phase

She reported that her periods were regular on the birth control pill, but has been irregular since she discontinued taking them. She reports having periods every 6-7 weeks.

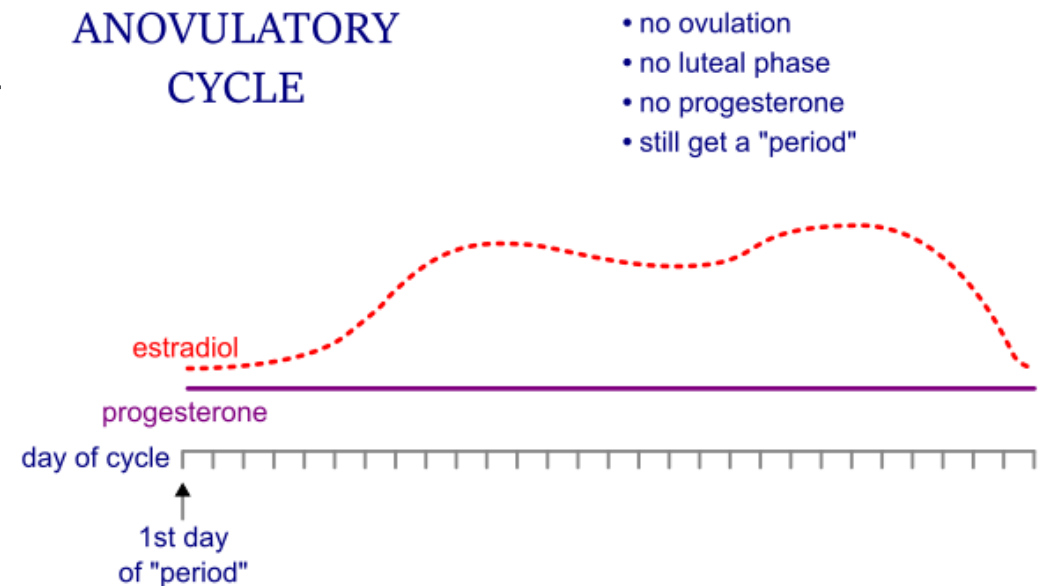
Interpret

What are the possible causes of extended menses irregularity?

- ✓ This patient may have **anovulatory cycles** due to use of **OCPs**.
- ✓ Anovulatory cycles are menstrual cycles without ovulation due to insufficient LH surge.
- ✓ Anovulatory cycles are common for the first year after the onset of puberty, before the onset of the menopause, females using hormonal birth control or OCPs being underwe



gnifican



Common Causes of Anovulation and Ovulatory Dysfunction



Polycystic ovarian syndrome (PCOS)



Too low body weight



Extreme exercise



Extremely high levels of stress



Hyperprolactinemia



Thyroid dysfunction (hyperthyroidism)



Perimenopause, or low ovarian reserves



Premature ovarian failure

9- What are the possible causes of extended menses irregularity in Laila?

The post pill amenorrhea period could extend up to 6 months and if more than this period there is probably another cause and the first cause to think about is hyperprolactinemia

She has been taking **Imipramine** for the last year.

Could drugs affect female fertility?

Imipramine is the least antidepressant drug affecting fertility compared to:

- other antidepressants as SSRI

or

- antipsychotics as risperidone

that increase serum prolactin level ☐
inhibit ovulation

Laila is 160cm in height and weighs 90 kilos.

What is Laila BMI?

What is its clinical significance?

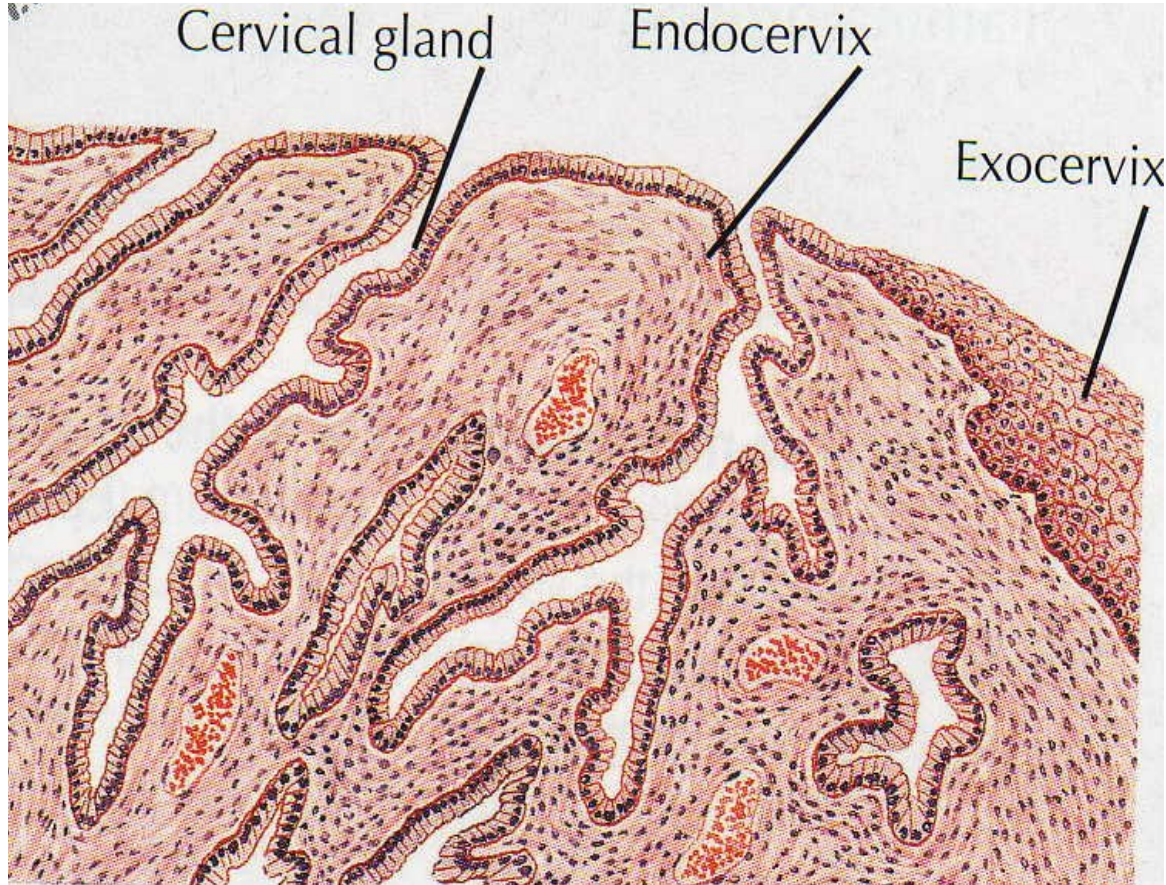
- High BMI may be associated with anovulation and conditions as polycystic ovarian syndrome

Pelvic exam reveals normal genitalia, well-estrogenized vaginal vault mucosa and cervical mucus consistent with the proliferative phase.

. What is meant by well-estrogenized vaginal mucosa?

What is the importance of cervical mucus?

Cervix

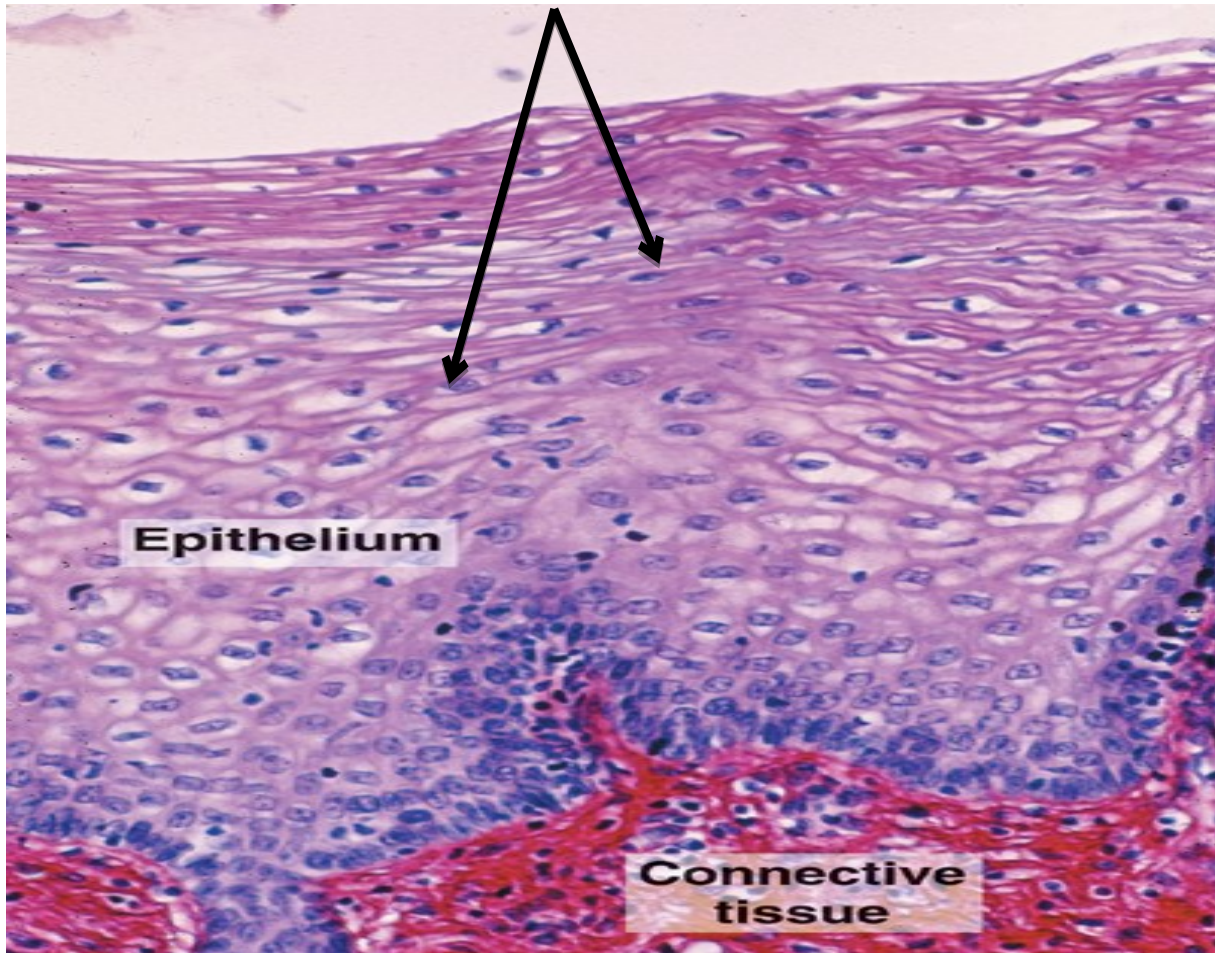


□ Cyclic changes of the cervix:

- The cervical mucosa is not shed during menstruation, but **cyclic changes** occur in the amount and viscosity of the cervical secretion.
- Under effect of estrogen, cervical mucus is watery.

Vagina

:Note
.Vacuolated epith



Under influence of estrogen:

- **↑ thickness of epithelium (multi-layered).**
- **↑ synthesis and storage of glycogen in superficial cells.**
- **Lamina propria is highly vascularized.**

What are the reproductive actions of estrogen and progesterone?

Biological Actions of Estrogens and Progesterone

Target Organ	Estrogen	Progesterone
Uterus	<ol style="list-style-type: none">1. Endometrial thickening2. Make cervical mucus thinner and more alkaline	<ol style="list-style-type: none">1. Increasing vascularization of the endometrium during the luteal phase2. Make cervical mucus more viscous
Vagina	<ol style="list-style-type: none">1. More cornified vaginal epithelium2. Induce synthesis of pheromones' in vaginal secretion	<ol style="list-style-type: none">1. Induces thick mucus secretions from the vaginal epithelium2. Causes epithelium to thicken and become infiltrated with leukocytes
Breast	<ol style="list-style-type: none">1. Promote growth and proliferation of mammary ducts2. Enlarge breasts at puberty3. Antagonize milk-producing effect of prolactin	<ol style="list-style-type: none">1. Increases growth of breast lobules and alveoli2. Induces differentiation of ductal tissue

The uterus is anteflexed and normal in size without masses or tenderness.

10- a. What is the normal position of the uterus?

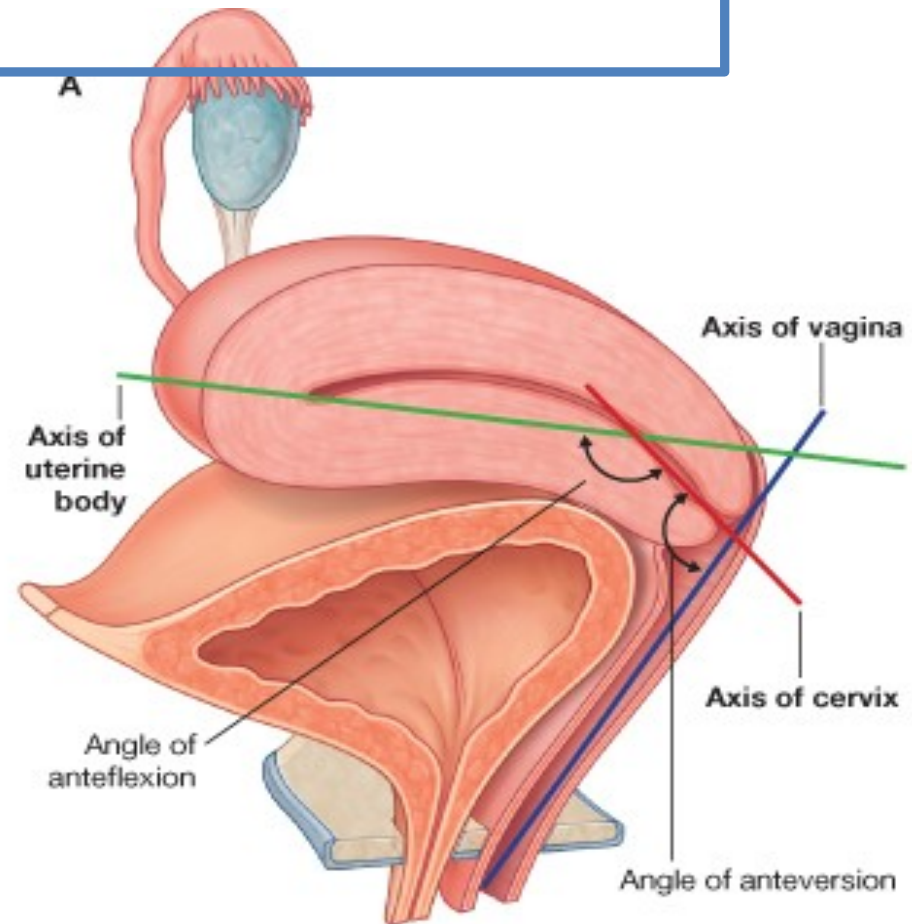
b. What are the factors that keep the uterus in its position?

a. What is the normal position of the uterus?

Anti verted & anti flexed

➤ **Angle of anteversion**: between longitudinal axis of uterus & axis of vagina (90)

➤ **Angle of anteflexion**: between body of uterus and cervix at level of internal os (170)
(body is bent forwards on cervix)



b. What are the factors that keep the uterus in its position?

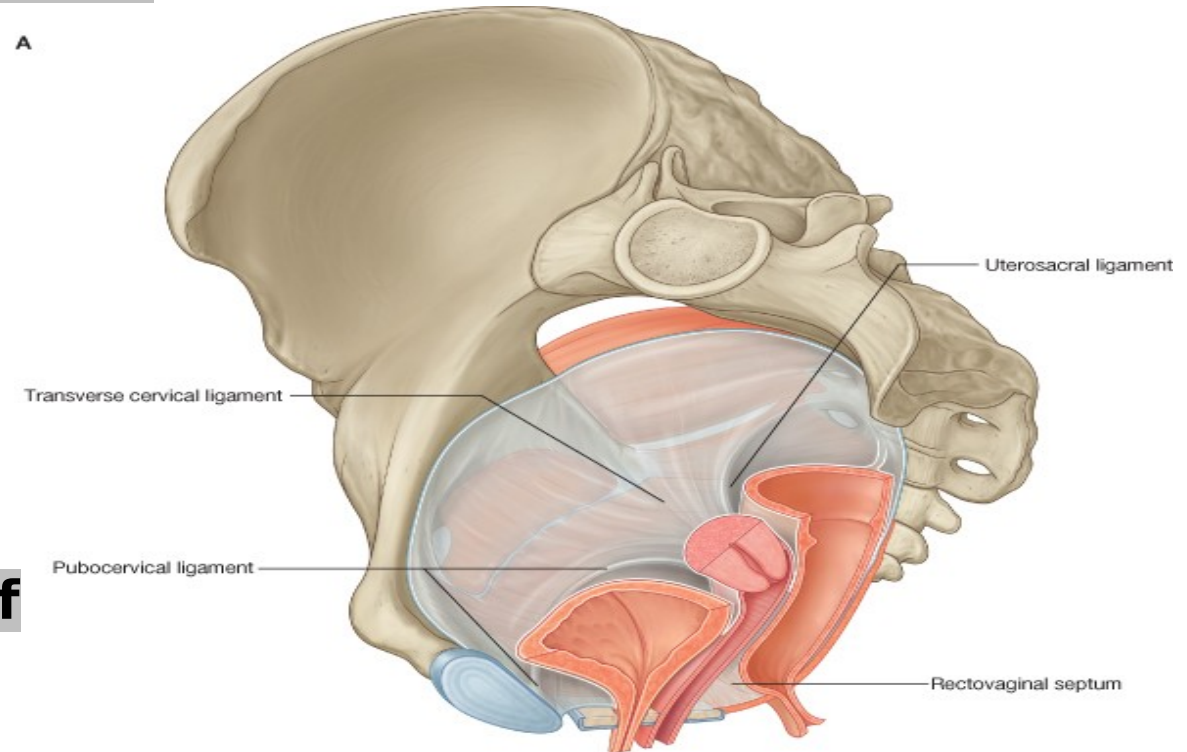
Peritoneal ligaments

- ❖ **Anterior ligament:** fold of peritoneum extends from anterior surface of uterus at junction of body & cervix to upper surface of urinary bladder
- ❖ **Posterior ligament:** fold of peritoneum extends from front of rectum to posterior vaginal fornix & superior to uterus

Fibro-muscular ligaments

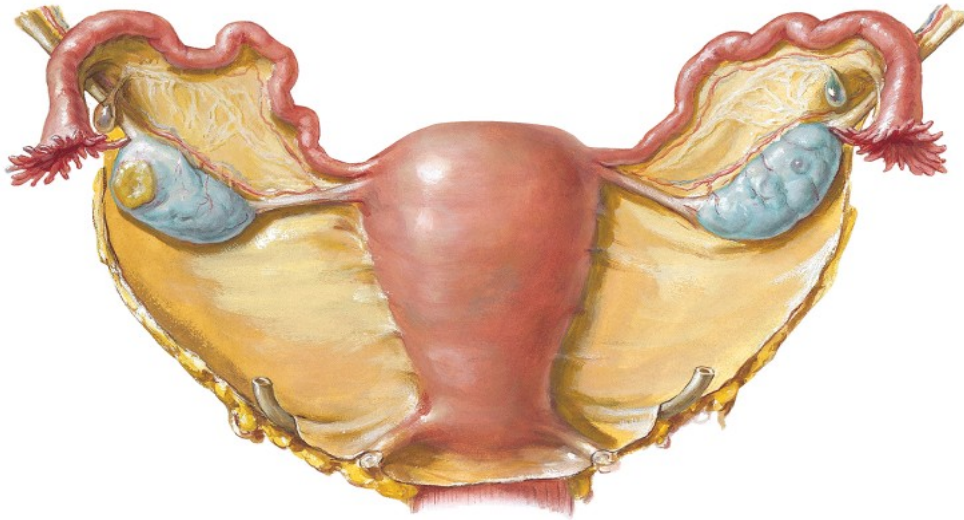
1-Transverse cervical: From side of cervix & upper part of vagina to side of pelvis & main support of uterus

2- Uterosacral: from posterolateral of cervix across side of rectum to middle of sacrum, pull cervix backwards against forward pull of round ligament



4- Ligaments of ovary:

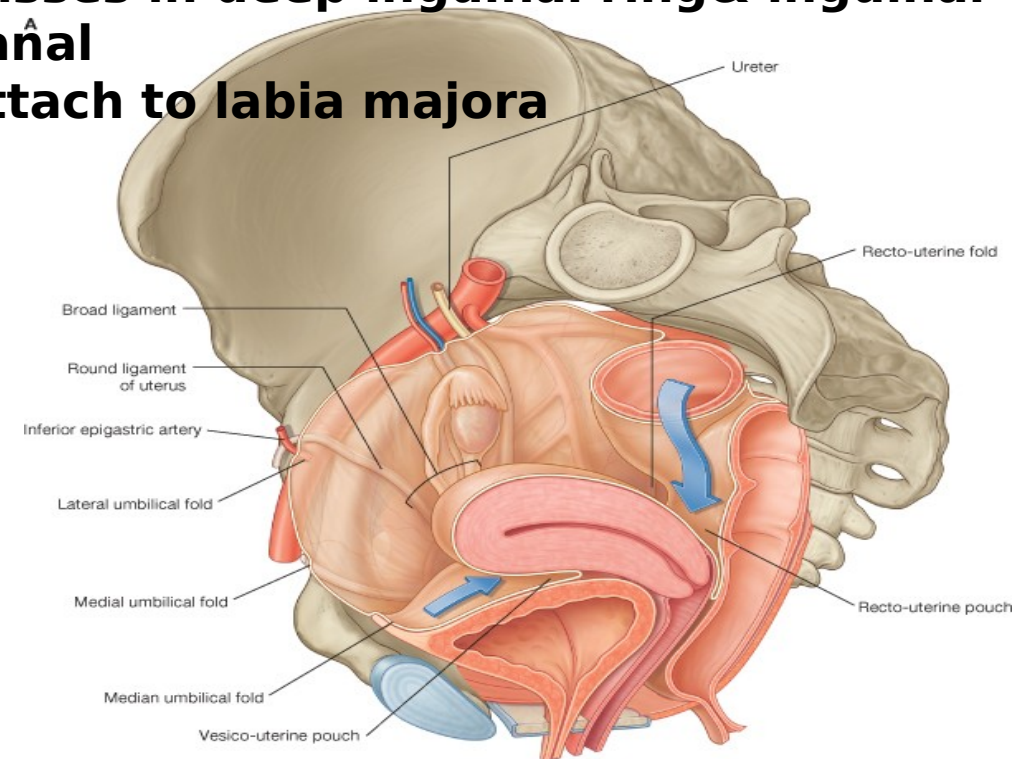
Extend from posterior surface of uterus below and behind uterine tube to the uterine end of ovary



5- Round ligament of uterus:

Extends below and in front uterotubal junction

- ☐ **Raises a ridge on lower surface of broad ligament**
- **Crosses on lateral wall of pelvis**
- ☐ **Hooks around inferior epigastric**
- ☐ **Passes in deep inguinal ring & inguinal canal**
- ☐ **Attach to labia majora**



11- How could you investigate this couple?

Investigations

- Male investigations

Semen analysis

- Female investigations

1. serum prolactin

2. FSH , LH

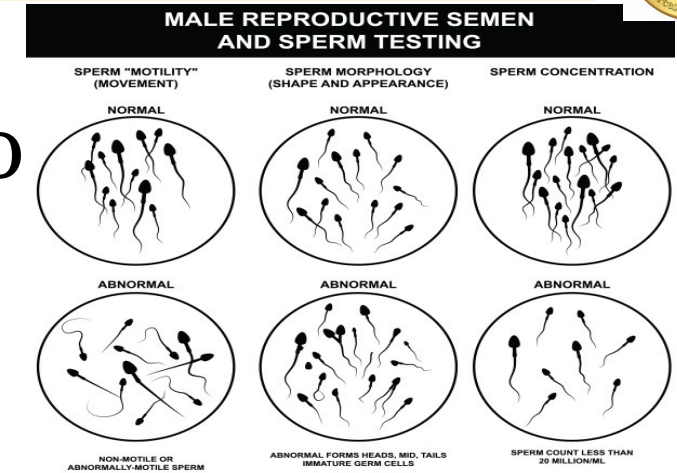
3. TSH , T3 , T4

Welcome Back

I want to get pregnant



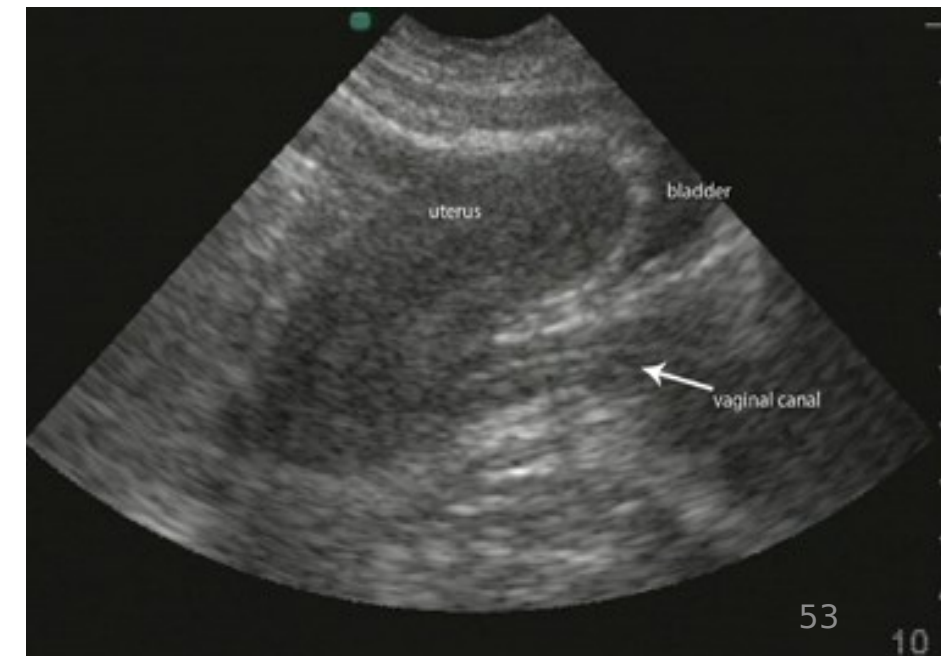
The doctor asked Roshdy to undergo **semen analysis**.



The doctor asked Laila to do serum

- Prolactin,
- FSH and LH levels
- TSH, T3, T4

The doctor asked for **pelvic ultrasonography**



I want to get pregnant



Results showed:

Total sperm number: 5 million spermatozoa per ejaculate

Total motility: progressive motility 30% or more motile

- Laila lab results:
- Prolactin: increased 200ng/ml
 - FSH and LH levels: normal
 - TSH, T3, T4: normal

The doctor asked for CT for Laila. She was found to have microadenoma and was given Dostinex



Discussion

The doctor asked Laila to do serum

- Prolactin,
- FSH and LH levels
- TSH, T3, T4

What is the significance of these hormones?

Significance of hormones

➤ Serum prolactin

according to our case this mostly a case of anovulation due to hyperprolactinemia represented by galactorrhea

➤ FSH , LH

as these are the dominant hormones responsible for regulation of the ovarian cycle

➤ TSH , T3 , T4

as any abnormality in thyroid hormones levels could affect menstruation and cause oligomenorrhea or menorrhagia

**How could you manage
this case?**

Management

The patient was given Dostinex (cabergoline) which is dopamine agonist to control hyperprolactinemia

12- What is the mechanism of action of dostinex?

**Laila was given Cabergoline
(Dostinex)**

**What is the mechanism of action of
cabergoline (Dostinex)?**

- **Cabergoline (Dostinex) is an ergot
derivative**

**It is a long-acting dopamine D2
receptors agonist □ inhibits prolactin
release.**



Although Bromocriptine is also a dopamine receptor agonist and can also inhibit prolactin release

But cabergoline is the drug of choice.

Why?

Bromocriptin

e:

- **Once daily**
- **Less potent**
- **More side effects**

Cabergoline :

- **Twice weekly**
- **More potent**
- **Less side effects**

N. B:

Cabergoline is effective in many cases of pituitary tumors resistant to

Take home message

Basic Work-up for Infertility

- **Semen analysis:**
 - semen volume: 1.5ml or more
 - pH: 7.2 or more
 - **sperm concentration:** 15 million spermatozoa per ml or more
 - **total sperm number:** 39 million spermatozoa per ejaculate or more
 - **total motility:** 40% or more motile or 32% or more with progressive motility
 - vitality: 58% or more live spermatozoa
 - **sperm morphology** (percentage of normal forms): 4% or more

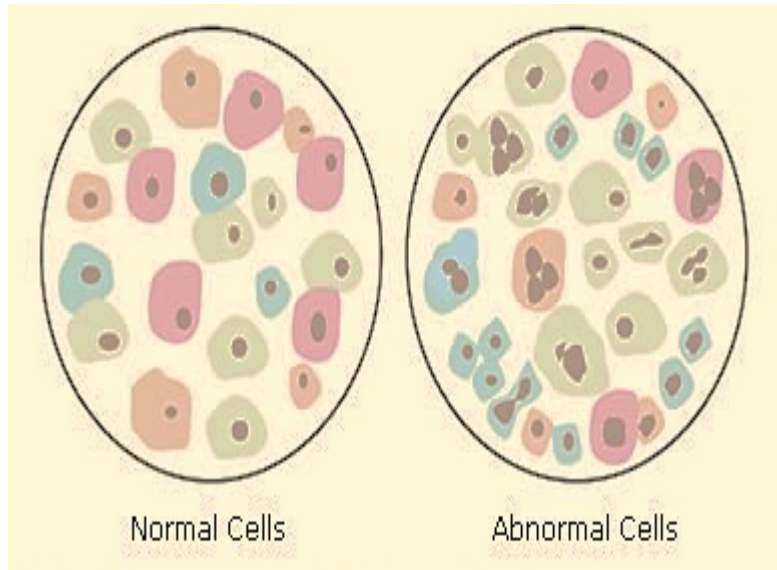
Thank
you



Laila has no history of sexual transmitted diseases and **no abnormal Paps.**

What is the importance of Paps?

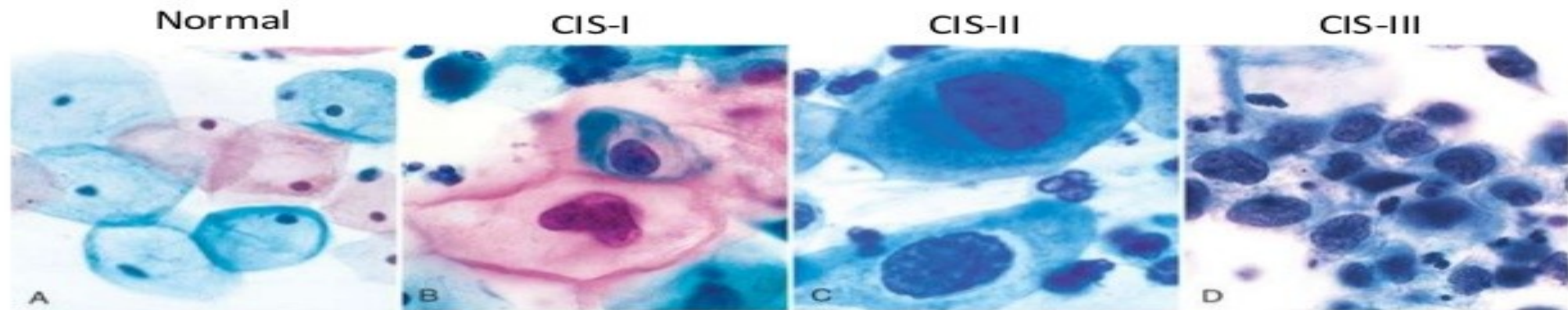
Results of Pap Smear



Normal: no abnormal cells were seen.

Atypical cells: the cells are not clearly normal or abnormal. This may be due to HPV, vaginal infections, or a processing issue in the lab.

Abnormal: the cells are precancerous, or dysplastic.



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There is Progressive reduction of size of Cytoplasm, and increase in Nuclear Cytoplasm Ratio as the grade of lesion progresses, which reflects there is loss of cellular differentiation on the surface of cervical lesion